

### REMARKS

Claims 27-43 and 45-64 are under examination in this case. Claims 27-28, 35-36, and 60-64 stand rejected under 35 U.S.C. § 112, second paragraph, and claims 31, 36, 46, and 47 stand rejected under 35 U.S.C. § 112, first paragraph. In addition, claims 27-30, 32-43, 45-47, and 60-64 stand rejected under 35 U.S.C. § 102(e), and claims 46-59 stand rejected under 35 U.S.C. § 103(a). Claim 30 stands objected to. Each of these issues is addressed below.

### Amendments

The specification has been amended to incorporate priority application information; this information is identical to that listed on the Official Filing Receipt. In addition, claim 27 has been amended to incorporate the limitation of original claim 58, now cancelled. Claims 28, 36, and 37 have been amended to clarify claim language or change claim dependencies. New claim 65 has been added; this claim finds support in the specification at page 9, lines 11-12. Claims 30-32, 35, 44, 46, 48, 50, 52, 54, 56, 58, and 60-64 have been cancelled. For the record, Applicants disagree with the rejections applied in this case and reserve the right to pursue all cancelled subject matter in this or future, related applications. No new matter has been added by the amendments.

### Claim Objections

Claim 30 stands objected to as being in improper dependent form. This claim has been cancelled, and the objection is moot.

### Rejections under 35 U.S.C. § 112, second paragraph

Claims 27-28, 35-36, and 60-64 stand rejected under 35 U.S.C. § 112, second paragraph. Claims 35 and 60-64 have been cancelled, and as applied to these claims the rejection is moot. As applied to all other claims, as amended, the rejection is respectfully

traversed.

Claim 27 stands rejected as being indefinite in its recitation of “purifying AAV and/or AAV particles.” The Office contends that the two terms are used interchangeably.

Claim 27 has been amended to recite only the term “AAV particles.” This basis for the rejection may be withdrawn. Claim 27 stands further rejected based on the assertion that the term “using” does not constitute an active method step. This term has been removed and replaced with the term “purifying.” This basis for the rejection of claim 27 should also be withdrawn.

Claim 28 stands rejected as being indefinite because the term “improvement” is a relative term. To clarify, claim 28 now specifies that the improvement in purification of the mutant AAV particles is relative to purification of wild-type AAV. This basis for the rejection may be withdrawn.

Claim 36 is rejected as indefinite on the basis that it is unclear whether the term “antibody epitope” refers to an epitope that binds to an antibody or an epitope presented by an antibody. This rejection is respectfully traversed. Applicants’ specification makes clear that this term is used to indicate an epitope *presented by* an antibody. For example, at page 7, lines 33-37, it states:

The inserted amino acid can, in particular, be selected from the following group: a ligand or a receptor or the receptor of a ligand, an antibody or part of an antibody, in particular an antibody epitope, an antigen or antigen epitope.

Thus, an antibody epitope is “part of an antibody” and must therefore be an epitope presented by the antibody. Moreover, in the passage from the specification presented above and in claim 36, an alternative amino acid insertion is an “an antigen epitope,” that is, an epitope from an antigen. The use of the alternative term antigen epitope further indicates that an “antibody epitope” is an epitope portion of an antibody. This basis for the rejection may be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 31, 36, 46, and 47 stand rejected under 35 U.S.C. § 112, first paragraph. Claims 31 and 46 have been cancelled. As applied to claims 36 and 47, this rejection is respectfully traversed.

Claim 36 stands rejected as lacking enablement. The Office contends that insertions of large amino acid sequences are not enabled by the present specification and certain of the sequences listed in claim 36 would not be workable on that basis. Applicants respectfully disagree. Applicants have identified particular AAV sites amenable to amino acid insertion and have recited those sites in independent claim 27. Applicants have also provided in their specification exemplary methods for making AAV particles having insertions and for testing those particles for infectivity (see, for example, pages 16-26). To the extent the size of an insertion might be problematic (which Applicants do not concede), those insertions would readily be identified. In view of this teaching in the specification, it would be well within the skill of one in the art to produce mutant AAV particles capable of infectivity and exhibiting improved purification characteristics. This basis for the rejection may be withdrawn.

Claim 47 also stands rejected as lacking enablement on the basis that the claimed N-terminus would not be amenable to mutations affecting purification as this region is located internal to the viral particle. As support for this assertion, the Office cites Hoque et al. (BBRC 266:371-376, 1999). This basis for the rejection is respectfully traversed. As an initial matter, Applicants take no position on the correctness of the conclusions drawn in Hoque, as the position of the AAV N-terminus is not dispositive to the issue of enablement for claim 47. As amended, independent claim 27 recites particular AAV sites amenable to mutations that can result in improved purification properties, as required by the claims. Dependent claim 47 simply recites “additional mutations,” the purpose of which can relate to any AAV property, including a property, for example, unrelated to purification. Accordingly, the location of the N-terminus and its relationship to

purification properties is not central to the issue of enablement of this claim. This basis for the rejection should be withdrawn.

#### Rejection under 35 U.S.C. § 102(e)

Claims 27-30, 32-36, 38-43, 45-47, and 60-64 stand rejected under 35 U.S.C. § 102(e) as being anticipated by US Patent 6,491,907. Claims 30, 32, 35, 46, and 60-64 have been cancelled. As applied to current claims 27-29, 33, 34, 36, 38-43, 45, and 47, this rejection is respectfully traversed. Independent claim 27, on which all other rejected claims depend, has been amended to include the limitation of original claim 58. As indicated, claim 58 is free of this rejection. Accordingly, the rejection as applied to current claims 27-29, 33, 34, 36, 38-43, 45, and 47 should be withdrawn.

In addition, the Office appears to have rejected claim 37 as being anticipated by US Patent 5,276,136. Again, claim 37 now includes the limitation (through independent claim 27) of original claim 58, a claim that is free of this rejection. This basis for the rejection, to the extent that it has been applied under § 102 (rather than § 103 as stated in the Office Action) may also be withdrawn.

#### Rejections under 35 U.S.C. § 103(a)

Claims 46-59 stand rejected under 35 U.S.C. § 103(a). Claims 48-57 stand rejected as being unpatentable over US Patent 6,491,907 in view of Spear et al. (J. Virol., 1977, pp. 627-634). Claims 46 and 47 stand rejected as being unpatentable over US Patent 6,491,907 in view of Yang et al. (Hum. Gene Ther. 9:1929-1937, 1998). And claims 58-59 stand rejected as unpatentable over US Patent 6,491,907 in view of Ruffing et al. (J. Gen. Virol. 75:3385-3392, 1994).<sup>1</sup> Claims 46, 48, 50, 52, 54, 56, and 58 are cancelled. As applied to the remaining, amended claims, this rejection is respectfully

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<sup>1</sup> At page 10, under the heading Claim Rejections – 35 USC § 102, the Office Action also indicates without further comment that claim 37 is rejected under 35 U.S.C. § 103(a) as being unpatentable over US Patent 6,491,907 in view of US Patent 5,276,136. Applicants have treated this passage in the Office Action as an error.

traversed.

Amended claim 27, as indicated above, now includes the limitation of original claim 58, a claim found to be free of the § 103(a) rejections based on US Patent 6,491,907 in combination with either Spear or Yang. These rejections, as applied to claims 46-57 should be withdrawn.

The rejection of claims 58 and 59 over US Patent 6,491,907 in view of Ruffing, as this rejection may relate to claims 27 and 59, is respectfully traversed. The '907 patent does not disclose the specific mutations recited in claim 27 as recognized by the Examiner, and Ruffing does not cure this deficiency. Claim 27 requires AAV capsid assembly, as the claim now recites the purification of "AAV particles." Ruffing does not provide such an AAV structural protein. As stated by Ruffing in the Abstract (second last sentence; emphasis added):

Analysis of virus formation and subcellular localization of the capsid proteins revealed a defect of the mutant capsid proteins in capsid assembly.

See also page 3391, left col., last para. In addition, Ruffing makes clear that the mutations disclosed in that reference are localized to the C-terminus of the capsid protein at positions distinct from those claimed by Applicants. As indicated in Ruffing at page 3386, first column, third full paragraph, Ruffing's mutations occur at position 4242 ("pTAV-p") and position 4233-4242 ("pTAV-d"). For illustration purposes, these positions are underlined in the attached AAV sequence (Exhibit I). Also shown in Exhibit I are the mutation sites recited in claim 27. Applicants' sites, which are indicated by highlighting, are clearly distinct from the Ruffing mutations. In view of the above distinctions, Ruffing adds little or nothing to the teaching of the '907 patent. No *prima facie* case of obviousness exists for the present claims, and the § 103 rejection should be withdrawn.

Information Disclosure Statement

Applicants note that the Form PTO 1449 that was submitted with an Information Disclosure Statement filed on January 31, 2006 has not been initialed and returned, and hereby request that it be initialed and returned with the next Office action.

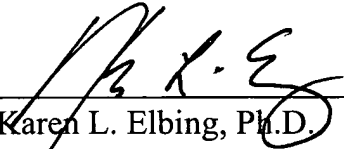
CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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